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REDUCED MORTALITY IN PEDIATRIC BURN PATIENTS TREATED WITH AUTOLOGOUS CULTURED SKIN SUBSTITUTES DURING A FDA INTEGRITY HOLD

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Abstract

INTRODUCTION. Prompt and stable wound closure remains a limiting factor for survival of extensive, deep burn injuries. Hypothetically, early replacement of both dermal and epidermal tissues may provide stable wound closure and reduce mortality from burns greater than 50% of the total body surface area (TBSA).

METHODS. Sixteen pediatric subjects were enrolled by Compassionate Use Enrollment into IDE G980023 during an Integrity Hold from 2007-2010. Age (mean±SEM) was 6.1±1.2 years old, and full-thickness burns were 77.9±2.8% TBSA. Split-thickness skin biopsies were collected for culture of autologous keratinocytes and fibroblasts, cells were combined with collagen-GAG scaffolds, and cultured skin substitutes (CSS) were incubated to promote formation of epidermal barrier. CSS and meshed, split-thickness skin autografts (AG) were applied to paired wound sites, and applications continued until wound closure was completed. Mortality data for burn patients of 0-19.9 years of age, and burns of 50-99% TBSA were obtained from the 2012 National Burn Repository (NBR), and averaged for comparison with mortality data from the IDE.

RESULTS. One subject expired during preparation of CSS. The remaining 15 subjects received CSS, and survived for an overall mortality rate of 6.25%. This mortality rate is statistically lower (p=0.037; one-sample z-test) than the average rate of 30.3% reported in the NBR for patients of comparable age and magnitude of injury.

CONCLUSION. These results demonstrate a lower mortality rate than currently reported in the NBR for pediatric patients with deep, extensive burn injuries, and suggest that autologous CSS may contribute to reduced mortality in patients with life-threatening burn injuries.

Introduction

Mortality from burns increases proportionately with the extent and depth of burn injury, and is greater in the very young and elderly populations[1]. A limiting factor in survival of deep, extensive burns is prompt and stable wound closure that restores the protective functions against infection and fluid loss that contribute to sepsis and physiologic instability[2]. To address the need for early wound closure, an autologous cultured skin substitute was studied under Investigational Device Exemption (IDE G980023) from the US Food and Drug Administration Center for Devices and Radiologic Health (CDRH)[3]. In 2007, an Integrity Hold was placed on the IDE for deficiencies in study performance and regulatory oversight. However, CDRH permitted continued enrollment of subjects under the Compassionate Use Enrollment mechanism through 2010. This report describes results of mortality in subjects enrolled in IDE G980023 from 2007-2010.

Methods

Subjects with burns greater than 50% of the Total Body Surface Area (TBSA) were enrolled into a protocol approved by the Institutional Review Board of the University of Cincinnati, and into IDE G980023 approved by the Center for Devices and Radiologic Health (CDRH) at the US Food and Drug Administration. Sixteen subjects reported here were enrolled by Compassionate Use Enrollment from 2007-2010 during an Integrity Hold placed on the IDE by CDRH. The study was closed to enrollment in 2010. Mortality was not a study end point in the IDE.

Cultured skin substitutes were prepared as described previously[3], applied to excised, full-thickness burns, and irrigated with non-cytotoxic antimicrobial agents[4] for five days. On post-operative day 5, wet dressings were removed and open areas on wounds were treated with equal parts Neosporin, Bactroban and Nystatin until closed after which the healed skin was moisturized with Eucerin.

Mortality was evaluated by comparison of this 16-subject, pediatric population with data from 1008 entries in the 2012 National Burn Repository[5] from burn patients of Birth-19.9 years of age, and burn areas ranging from 50.0% to >90.0%. The patient populations were not matched for other criteria. Data were tested statistically by a one-sample z-test, and significance was accepted at the 95% confidence level.

Results

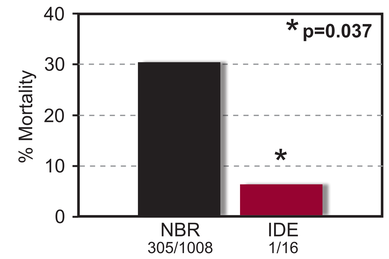
TABLE 1 Mortality Data from the 2012 National Burn Repository (NBR)

%TBSA burned: AGE IN YEARS		50-59.9	60-69.9	70-79.9	80-89.9	>90	TOTALS
Birth-0.9	Died	21	22	21	19	33	116
	Total	73	49	42	27	36	227
	% Mortality	28.8%	44.9%	50.0%	70.4%	91.7%	51.1%
1-1.9	Died	3	6	2	1	3	15
	Total	18	21	10	4	4	57
	% Mortality	16.7%	28.6%	20.0%	25.0%	75.0%	26.3%
2-4.9	Died	13	4	7	18	10	52
	Total	66	43	28	30	22	189
	% Mortality	19.7%	9.3%	25.0%	60.0%	45.5%	27.5%
5-15.9	Died	6	10	8	24	21	69
	Total	117	86	58	49	35	345
	% Mortality	5.1%	11.6%	13.8%	49.0%	60.0%	20.0%
16-19.9	Died	6	6	5	14	22	53
	Total	64	42	27	24	33	190
	% Mortality	9.4%	14.3%	18.5%	58.3%	66.7%	27.9%
Totals	Died	49	48	43	76	89	305
	Total	338	241	165	134	130	1008
	% Mortality	14.5%	19.9%	26.1%	56.7%	68.5%	30.3%

TABLE 2 Mortality Data from IDE G980023 [2007-2011]

Subject	yrs of age	%FT burn	Mortality
1	17.0	80.3%	0
2	10.0	94.0%	0
3	2.0	90.0%	0
4	2.0	68.0%	0
5	1.5	58.8%	0
6	10.0	65.0%	0
7	2.0	92.0%	1
8	10.0	64.3%	0
9	2.5	70.5%	0
10	3.0	75.5%	0
11	3.0	69.9%	0
12	7.0	84.5%	0
13	13.0	82.5%	0
14	2.0	95.0%	0
15	4.0	81.5%	0
16	8.0	74.3%	0
Died/Total			1/16
Mean	6.1	77.9%	6.25%
SEM	1.2	2.8%	
Range	1.5-17.0	58.8-95.0%	

FIGURE 1 Mortality data from the 2012 NBR and IDE G980023



Conclusion and Discussion

Results from this study indicate that:

- Treatment of pediatric patients with burns of greater than 50% TBSA with autologous CSS reduces mortality.
- Assessment of mortality should be added to future studies of CSS for burns.

Acknowledgements

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